

| | | | | | |
|--|---|-------------------------------|--|----------------------------------|--|
| Subt. For, PTO-1449 | | Docket Number HYZ-030CPON3 | | Application Number 09/777,526 | |
| INFORMATION DISCLOSURE IN AN APPLICATION (Use several sheets if necessary) | | | | Applicant Agrawal et al. | |
| | | | | Filing Date February 6, 2001 | |
| Sheet | 2 | OF | | Group Art Unit 1635 | |

| Other Documents (Including Author, Title, Date Pertinent Pages, Etc.) | | |
|---|-------------|--|
| <i>pg</i> | A1 | Agrawal et al., "Oligodeoxynucleoside phosphoramidates and phosphorothioates as inhibitors of human immunodeficiency virus", <i>Proc. Natl. Acad. Sci. USA</i> , Vol. 85, pp. 7079-7083 (1988) |
| | A2 | Agrawal et al., "Inhibition of human immunodeficiency virus in early infected and chronically infected cells by antisense oligodeoxynucleotides and their phosphorothioate analogues", <i>Proc Natl Acad Sci U S A.</i> , Vol. 86, pp. 7790-4 (1989) |
| | A3 | Agrawal et al., "Site-specific excision from RNA by RNase H and mixed-phosphate-backbone oligodeoxynucleotides", <i>Proc Natl Acad Sci U S A.</i> , Vol. 87, pp. 1401-5 (1990) |
| | A4 | Agrawal et al., "Pharmacokinetics, biodistribution, and stability of oligodeoxynucleotide phosphorothioates in mice", <i>Proc Natl Acad Sci U S A.</i> , Vol. 88, pp. 7595-9 (1991) |
| | A5 | Agrawal, "Antisense oligonucleotides as antiviral agents", <i>Trends in Biotechnol.</i> , Vol. 10, pp. 152-158 (1992) |
| | A6 | Agrawal, "Functionalization of oligonucleotides with amino groups and attachment of amino specific reporter groups", <i>Methods in Molecular Biology: Protocols for Oligonucleotide Conjugates</i> (Agrawal, Ed.), Humana Press., pp. 93-120 (1994) |
| | <i>X</i> A7 | Agrawal, et al., "Pharmacokinetics and Bioavailability of Antisense Oligonucleotides Following Oral and Colorectal Administrations in Experimental Animals", <i>Handbook of Experimental Pharmacology, Volume 131: Antisense Research and Application</i> (Crooke, Ed.), Springer-Verlag, pp. 525 - 543 (1998) |
| | A8 | Bayever et al., "Systemic administration of a phosphorothioate oligonucleotide with a sequence complementary to p53 for acute myelogenous leukemia and myelodysplastic syndrome: initial results of a phase I trial", <i>Antisense Res Dev.</i> Vol. 3, pp. 383-90 (1993) |
| | B1 | Boutorine et al, "Effect of derivatization of ribophosphate backbone and terminal ribophosphate groups in oligoribonucleotides on their stability and interaction with eukaryotic cells", <i>Biochimie</i> Vol. 76, pp. 23-32 (1994) |
| | B2 | Ceruzzi et al., "The Intracellular and Extracellular Fate of Oligodeoxyribonucleotides in Tissue Culture Systems", <i>Nucleosides and Nucleotides</i> 8 (5&6), 815-8 (1989) |
| <i>X</i> | B3 | Craig et al., "Patent Strategies in the Antisense Oligonucleotide Based Therapeutic Approach", <i>Exp. Opin. Ther. Patents</i> , Vol. 7, No. 10, pp.1175-1182 (1997) |
| | B4 | Crooke, S. T., "Progress in the Development of Antisense Drugs", <i>Exp. Opin. Invest. Drugs</i> , Vol. 5, No. 8, pp. 1047-1052 (1996) |
| | B5 | Egli et al., "Structural Origins of the High RNA Affinity of 2'-O-Methoxyethyl RNA: Crystal Structure of an All-Modified 2'-O-MOE RNA Dodecamer Duplex, <i>Antisense</i> 98: Targeting the Molecular Basis of Disease, October 8-9, 1998 |
| <i>Ref</i> | B6 | Furdon et al., "RNase H cleavage of RNA hybridized to oligonucleotides containing methylphosphonate, phosphorothioate and phosphodiester bonds", <i>Nucleic Acids Res.</i> , Vol. 17, No. 22, pp. 9193-204 (1989) |

| | |
|--|-----------------------------------|
| EXAMINER <i>Pura Hill</i> | DATE CONSIDERED <i>6/26/03</i> |
| EXAMINER: Initial if citation is considered, whether or not citation is in conformance with MPEP § 609: Draw Line through citation if not conformance and not considered. Include copy with next communication to applicant. | |

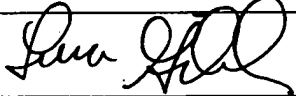
| | | | |
|--|---|---------------------------------|----------------------------------|
| Subt. For, PTO-1449 | | Docket Number HYZ-030CPCOR3 | Application Number 09/777,526 |
| INFORMATION DISCLOSURE IN AN APPLICATION (Use several sheets if necessary) | | Applicant Agrawal et al. | |
| | | Filing Date February 6, 2001 | Group Art Unit 1635 |
| Sheet | 3 | OF | |

| | |
|-----|--|
| B7 | Galderisi et al., "Antisense oligonucleotides as therapeutic agents", <i>J. Cell. Physiol.</i> , Vol. 181, pp. 251-57 (1999) |
| C1 | Hughes et al., "Radiolabeling of methylphosphonate and phosphorothioate oligonucleotides and evaluation of their transport in everted rat jejunum sacs", <i>Pharm Res.</i> , Vol. 12, No. 6, pp. 817-24 (1995) |
| C2 | Inoue et al., "Sequence-dependent hydrolysis of RNA using modified oligonucleotide splints and RNase H", <i>FEBS Lett.</i> , Vol. 215, No. 2, pp. 327-30 (1987) |
| C3 | International Business Communications, IBC, 's Fourth Annual International Symposium on Oligonucleotide- and Gene Therapy-Based Antisense Therapeutics with New Applications for Genomics, February 6-7 1997 |
| C4 | International Business Communications, IBC, 's Sixth International Conference on Oligo-Therapeutics, Molecular Tools and Novel Therapeutic Strategies, May 1999 |
| C5 | Isis Pharmaceuticals, Inc., <i>Antisense 97: Targeting the Molecular Basis of Disease</i> , Nature Biotechnology Conference, May 1-2 1997 |
| C6 | Isis Pharmaceuticals, "Orasense Joint Venture Announces Pivotal First Step in Development of Oral Formulation of Antisense Drugs", Press Release, June 5, 2000 |
| C7 | Iversen, "In vivo studies with phosphorothioate oligonucleotides: pharmacokinetics prologue", <i>Anti-Cancer Drug Des.</i> , Vol. 6, pp. 531-8 (1991) |
| C8 | Iversen, et al., "Pharmacokinetics of an antisense phosphorothioate oligodeoxynucleotide against rev from human immunodeficiency virus type 1 in the adult male rat following single injections and continuous infusion", <i>Antisense Res Dev.</i> , Vol. 4, pp. 43-52 (1994) |
| C9 | Kawasaki et al., "Uniformly modified 2'-deoxy-2'-fluoro phosphorothioate oligonucleotides as nuclease-resistant antisense compounds with high affinity and specificity for RNA targets", <i>J Med Chem.</i> , Vol. 36, No. 7, pp. 831-41 (1993) |
| C10 | Levin, "The Pharmacokinetics and Toxicity of Oligonucleotides: New Routes of Administration", <i>Antisense 98: Targeting the Molecular Basis of Disease</i> , Organized by Nature Biology, London, UK, October 8-9, 1998 |
| D1 | Martin, P. "Ein neuer Zugang zu 2'-O-Alkylribonucleosiden und Eigenschaften deren Oligonucleotide", <i>Helvetica Chimica Acta</i> , Vol. 78, pp. 486-504 (1995) |
| D2 | Metelev et al, "Study of Antisense Oligonucleotide Phosphorothioates Containing Segments of Oligodeoxynucleotides and 2'-O-Methyloligoribonucleotides", <i>Bioorganic & Medicinal Chemistry Letters</i> , Vol.4, No. 24, pp. 2929-2934 (1994) |
| D3 | Milligan et al., "Current concepts in antisense drug design", <i>J Med Chem.</i> , Vol. 36, No. 14, pp. 1923-37 (1993) |
| D4 | Orr, (Reported By), <i>Antisense 98: Targeting the Molecular Basis of Disease (Part III)</i> , Organized by Nature Biology, London, UK, October 8-9, 1998 |
| D5 | Quartin et al., "Number and distribution of methylphosphonate linkages in oligodeoxynucleotides affect exo- and endonuclease sensitivity and ability to form RNase H substrates", <i>Nucleic Acids Res.</i> , Vol. 17, No. 18, pp. 7253-62 (1989) |

| | |
|---|-----------------|
| EXAMINER | DATE CONSIDERED |
| EXAMINER: Initial if citation is considered, whether or not citation is in conformance with MPEP § 609: Draw Line through citation if not conformance and not considered. Include copy with next communication to applicant. | |

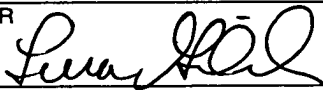
| | | | |
|--|---|---------------------------------|----------------------------------|
| Subt. For, PTO-1449 | | Docket Number HYZ-030CPCN3 | Application Number 09/777,526 |
| INFORMATION DISCLOSURE IN AN APPLICATION (Use several sheets if necessary) | | Applicant Agrawal et al. | |
| | | Filing Date February 6, 2001 | Group Art Unit 1635 |
| Sheet | 4 | OF | |

| | | |
|----|----|---|
| ER | D6 | Rapaport et al., "Antimalarial activities of oligodeoxynucleotide phosphorothioates in chloroquine-resistant <i>Plasmodium falciparum</i> ", <i>Proc Natl Acad Sci U S A.</i> , Vol. 89, pp. 8577-80 (1992) |
| | D7 | Sands, et al., "Biodistribution and metabolism of internally ³ H-labeled oligonucleotides. I. Comparison of a phosphodiester and a phosphorothioate", <i>Mol. Pharmacol.</i> , Vol. 45, pp. 932-43 (1994) |
| | D8 | Shibahara et al., "Site-directed cleavage of RNA", <i>Nucleic Acids Res.</i> , Vol. 15, No. 11, pp. 4403-15 (1987) |
| | E1 | Shibahara et al., "Inhibition of human immunodeficiency virus (HIV-1) replication by synthetic oligo-RNA derivatives," <i>Nucleic Acids Res.</i> , Vol. 17, No. 1, pp. 239-52 (1989) |
| | E2 | Sonveaux, "Protecting Groups in Oligonucleotide Synthesis" <u>Methods in Molecular Biology: Protocols for Oligonucleotide Conjugates</u> (Agrawal ed.), Humana Press, pp. 1-71 (1994) |
| | E3 | Stein et al., "Antisense oligonucleotides as therapeutic agents — is the bullet really magical?" <i>Science</i> , Vol. 261, pp. 1004-12 (August 1993) |
| | E4 | Takashima et al., "tau protein kinase I is essential for amyloid β -protein-induced neurotoxicity," <i>Proc Natl Acad Sci U S A.</i> , Vol. 90, pp. 7789-93 (1993) |
| | E5 | Tidd et al., "Partial protection of oncogene, anti-sense oligodeoxynucleotides against serum nuclease degradation using terminal methylphosphonate groups," <i>Br J Cancer.</i> , Vol. 60, pp. 343-50 (1989) |
| / | E6 | Tortora et al., "Oral antisense that targets protein kinase A cooperates with taxol and inhibits tumor growth, angiogenesis, and growth factor production," <i>Clin. Cancer Res.</i> Vol. 6, pp. 2506-12 (June 2000) |
| | E7 | Tseng et al., "Antisense oligonucleotide technology in the development of cancer therapeutics," <i>Cancer Gene Ther</i> , Vol. 1, No. 1, pp. 65-71 (1994) |
| | F1 | Uhlmann et al., "Antisense Oligonucleotides: A New Therapeutic Principle", <i>Chem. Rev.</i> Vol. 90, No. 4, pp. 543-584 (1990) |
| | F2 | Wang et al., "Antitumor activity and pharmacokinetics of a mixed-backbone antisense oligonucleotide targeted to the R1 α subunit of protein kinase A after oral administration," <i>Proc Natl Acad Sci U S A.</i> , Vol. 96, No. 24, pp. 13989-94 (1999) |
| | F3 | Wickstrom, E., "Oligodeoxynucleotide stability in subcellular extracts and culture media," <i>J Biochem Biophys. Methods</i> , Vol. 13, pp. 97-102 (1986) |
| | F4 | Wickstrom, E., "Strategies for administering targeted therapeutic oligodeoxynucleotides," <i>Trends Biotechnol.</i> , Vol. 10, pp. 281-7 (1992) |
| | F5 | Zamecnik, P., "History of Antisense Oligonucleotides", <u>Methods in Molecular Medicine: Antisense Therapeutics</u> (Agrawal, Ed.), Human Press, pp. 1-11 (1996) |
| ER | F6 | Zendegui, et al., "In vivo stability and kinetics of absorption and disposition of 3' phosphopropyl amine oligonucleotides", <i>Nucleic Acids Res.</i> , Vol. 20, No. 2, pp. 307-14 (1992) |

| | |
|--|----------------------------|
| EXAMINER  | DATE CONSIDERED 6/26/03 |
| EXAMINER: Initial if citation is considered, whether or not citation is in conformance with MPEP § 609: Draw Line through citation if not conformance and not considered. Include copy with next communication to applicant. | |

| | | | | | |
|--|---|-----------------------------|--|----------------------------------|--|
| Subt. For, PTO-1449 | | Docket Number HYZ-030CPO | | Application Number 09/777,526 | |
| INFORMATION DISCLOSURE IN AN APPLICATION (Use several sheets if necessary) | | | | Applicant Agrawal et al. | |
| | | | | Filing Date February 6, 2001 | |
| Sheet | 5 | OF | | Group Art Unit 1635 | |

| | | |
|----|----|---|
| Pg | F7 | Zhao, et al., "Comparison of Cellular Binding and Uptake of Antisense Phosphodiester, Phosphorothioate, and Mixed Phosphorothioate and Methylphosphonate Oligonucleotides", <i>Antisense Res. and Dev.</i> Vol. 3, pp. 53-66 (1993) |
| Pg | F8 | Zon, "Oligonucleotide Analogues and Potential Chemotherapeutic Agents", <i>Pharm. Res</i> Vol. 5, No. 9, pp. 539-49 (1988) |

| | |
|--|----------------------------|
| EXAMINER  | DATE CONSIDERED 6/26/03 |
| EXAMINER: Initial if citation is considered; whether or not citation is in conformance with MPEP § 609: Draw Line through citation if not conformance and not considered. Include copy with next communication to applicant. | |